

Global Evacuation of Burn Patients Does Not Increase the Incidence of Venous Thromboembolic Complications

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Background: Case-control studies have suggested that air travel may be a risk factor for the development of Venous Thromboembolism (VTE). Burned patients from the current war in Iraq and Afghanistan, are transported across three continents to our Burn Center with total ground and air transport time being approximately 24 hours spread over 3 days to 4 days. We hypothesized global evacuation results in increased VTE rates.

Methods: Retrospective review of 1,107 consecutive patients admitted to our

burn center from January 2003 to December 2005.

Results: In the time period evaluated, no detectible differences were found in incidence of VTE between air-evacuated soldiers and those admitted to our facility from South Texas (1.31% vs. 0.83%, $p = \text{ns}$). The air-evacuated soldiers were younger (26 ± 7 vs. 41 ± 19 , $p < 0.0001$) but had a higher incidence of inhalation injury (14.4% vs. 8.0%, $p < 0.0001$) and higher Injury Severity Score (10.9 ± 13.0 vs. 6.5 ± 9.2 , $p <$

0.0001). No difference in average percent total body surface area involvement was found (15.8 ± 19.4 vs. 15.5 ± 18.4 , $p = \text{ns}$). Overall, 11 of 1,107 (0.99%) burned patients developed VTE.

Conclusion: Prolonged global evacuation is not associated with increased risk of VTE.

Key Words: Injury, Burn, Trauma, Air travel, Deep vein thrombosis, Evacuation, Global, Pulmonary embolism, Thromboembolism, Venous.

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Because the first report of travel associated thrombosis by Dr. John Homans in 1954, there have been multiple studies linking long distance travel and thrombosis.¹ Most of the available data refer to air travel and suggest that a combination of travel-related factors to include prolonged stasis, dehydration, and hypobaric hypoxia are associated with increased risk. A recent comprehensive review by Chee and Watson,² suggested that the association between long-distance travel and thrombosis is weak at best. Travel times of greater than 8 hours appeared to confer the greatest risk for patients with additional individual risk factors such as presence of a coagulation disorder, malignancy, obesity, or recent surgery.²

In burn patients, the overall incidence of venous thromboembolism (VTE) has been estimated to range from 0.4% to 7%.^{3–6} It is unknown to what degree concomitant nonburn injury further increases this risk in this population. In hospitalized patients with major trauma without thromboprophylaxis the risk of deep venous thrombosis (DVT) is reported to be 40% to 80%.⁷

The United States Army Institute of Surgical Research Burn Center is the sole burn treatment facility in the Department of Defense serving active duty personnel. The United States Army Institute of Surgical Research also serves as the regional burn center in South Texas covering an area of 80,000 square miles. Patients burned locally are brought directly to our burn center via Emergency Medical Services. Patients burned outside city limits are referred through a centralized referral system and transported via, ground or air immediately to our burn center. Local transport times are usually under 4 hours. In contrast, military burn casualties from the war in Iraq and Afghanistan are transported across three continents, with one stop in Germany, to our burn center with total ground and air transport times exceeding 24 hours during 3 days to 6 days (See Fig. 1). The impact of long transport times in burn patients on the incidence of VTE is unknown. In addition to prolonged transport, many of the military burn casualties have concomitant traumatic injuries. The incidence of nonburn injury has already been reported to be significantly greater in combat-related burns when compared with local civilian burns (37% vs. 11%).⁸ In this study, we sought to evaluate the effect of global evacuation on the incidence of VTE in military burn casualties. We hypothesized that this population would have a higher incidence of VTE when compared with the local civilian burn population.

PATIENTS AND METHODS

We retrospectively analyzed data from our prospectively maintained trauma registry for all patients admitted to our

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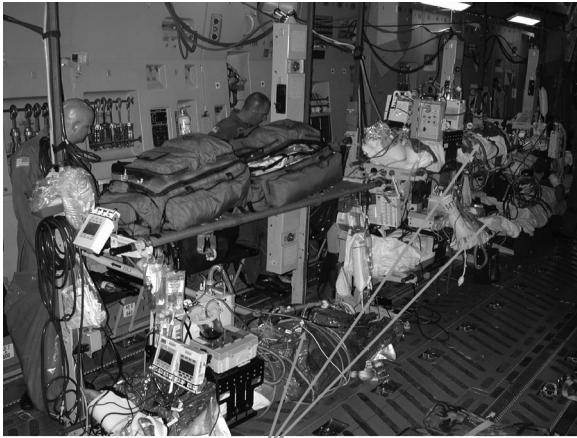
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Immobilized ICU patients

Fig. 1. Critically ill burn patients being air-evacuated.

burn center from the period of January 2003 to December 2005. Clinical data collected on each patient included age, sex, Injury Severity Score (ISS), presence of inhalation injury, percent total body surface area (TBSA) burned, number of hospital, intensive care unit (ICU) and ventilator days, number of major operative procedures, occurrence of DVT or pulmonary embolism (PE), and survival. During this time period, routine screening for VTE was not performed at our institution. Thus, studies were performed only if clinically indicated by patient symptoms (i.e., edema, shortness of breath, tachypnea, and unexplained hypoxemia, etc) and the providers' level of suspicion. Occasionally, venous thromboses were an incidental finding. All VTE events were recorded. The diagnosis of DVT was made either by duplex ultrasound or CT angiogram with lower extremity imaging. The diagnosis of PE was made by CT angiogram. None of the

diagnoses were made at autopsy. The incidence of VTE in air-evacuated soldiers was compared with the incidence in those admitted from the South Texas region. Approval for the study was given by the Brooke Army Medical Center Institutional Review Board before data collection.

Data were analyzed using SAS, version 8.1 (SAS Institute 1999). Univariate analysis was performed by using the Wilcoxon's rank sum test for continuous variables and the Fisher's exact test for categorical variables. Comparisons were made between patients with and without VTE. In addition, Pearson correlation coefficients were calculated to analyze the relationships between continuous variables, between dichotomous and continuous variables (point-biserial correlation), and between dichotomous variables exclusively (Phi). Multiple logistic regressions with stepwise selection were then performed to identify important predictors for VTE in the population. We chose variables with a p value of less than 0.2 in the univariate analysis and removed variables which correlated with others as final candidates for the logistic model. Hosmer-Lemeshow goodness-of-fit test was used to estimate the regression model fit. A receiver operating characteristic curve was constructed to assess the diagnostic performance of identified predictors.

RESULTS

Among 1,107 consecutive burn admissions in the 2-year period, 381 patients sustained their injury in Iraq and Afghanistan and were subjected to global evacuation across three continents. Overall, 11 of 1,107 (0.99%) burned patients developed VTE (See Fig. 2). We found no difference in the incidence of VTE between military burn casualties and those admitted to our facility from South Texas (1.31% vs. 0.83%, $p = 0.528$). A demographic comparison of the two groups is

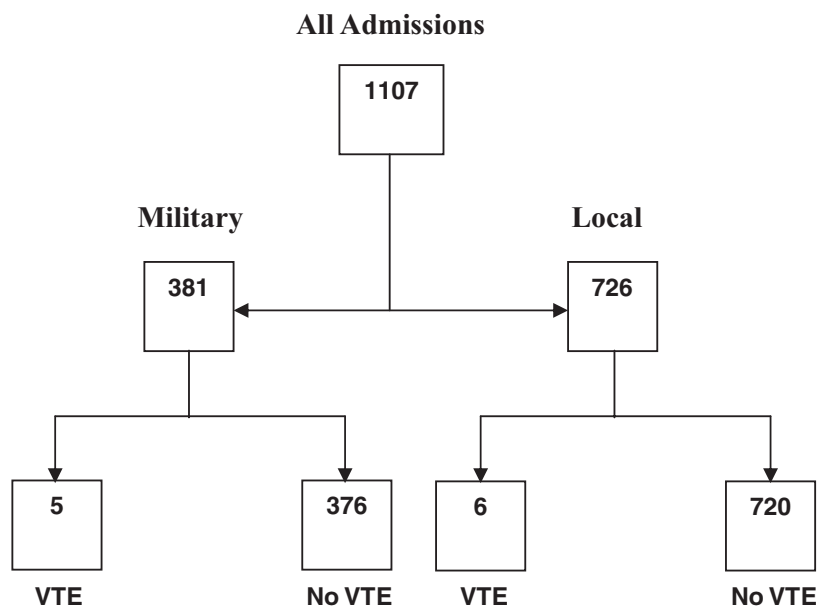
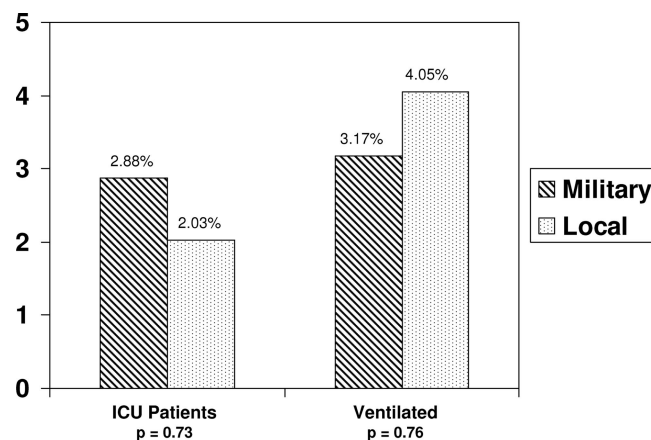


Fig. 2. Patient breakdown.

Table 1 Population Comparison

	Military	Civilian	<i>p</i>
Age (yrs)	26 ± 7	41 ± 19	<0.0001
Total % TBSA	15.8 ± 19.4	15.5 ± 18.4	ns
% TBSA full thickness burn	8.6 ± 17.1	5.2 ± 14.4	0.001
Inhalation	14.4%	8.0%	<0.0001
ISS	10.9 ± 13	6.5 ± 9.2	<0.0001
Major operative procedures	2.1 ± 2.8	1.7 ± 3.0	0.051
Hospital days	27 ± 45	17 ± 44	0.003
ICU days	23 ± 42	13 ± 23	0.005
Ventilator days	13 ± 22	13 ± 23	ns

**Fig. 3.** A comparison of VTE incidence when comparing military casualties versus local patients among high risk patients.

shown in Table 1. There were no cases of heparin-induced thrombocytopenia during this period. The incidence of VTE when comparing military to local patients among just the ICU patients ($N = 434$, 2.88% vs. 2.03%, $p = 0.73$) were no different. The VTE incidence among ventilated patients ($N = 274$, 3.17% vs. 4.05%, $p = 0.76$) were also no different (See Fig. 3).

Patients who developed VTE ($N = 11$) were not significantly older (mean age, 35.7 ± 17.2 vs. 31.7 ± 11.0 , $p = 0.689$) but had significantly larger percent TBSA burns (31.8 ± 24.2 vs. 15.3 ± 18.1 , $p = 0.012$), higher ISS (22.6 ± 13 vs. 8.9 ± 11.9 , $p < 0.0001$), than those who did not. Among those admitted to the ICU ($N = 434$) and placed on mechanical ventilation ($N = 274$), patients who developed VTE had a significantly higher mean ICU stay (38.4 ± 27.6 vs. 17.8 ± 32.1 , $p = 0.002$) and spent more time on the ventilator (26.5 ± 32.0 vs. 15.0 ± 23.8 , $p = 0.021$) than patients without VTE (See Table 2).

Of the 11 patients who were diagnosed with VTE, 5 patients had both PE and DVT, whereas the other 6 had lower extremity DVT (See Table 2). Ten of these patients were diagnosed via, helical computed tomography whereas only one was diagnosed via, lower extremity ultrasound. Venous thromboses were detected incidentally on two patients who were undergoing contrast study for another indication (See Table 3). One patient could be categorized as being obese ($>30\%$ above ideal body weight [IBW]). None of the patients

Table 2 Demographic Comparison Between Patient With VTE vs. no VTE

	VTE	No VTE	<i>p</i>
Age (yrs)	31.7 ± 11.0	35.7 ± 17.2	0.689
%TBSA	31.8 ± 24.2	15.2 ± 18.1	0.012
ISS	22.6 ± 13.0	8.9 ± 11.9	<0.0001
ICU Days ($N = 424$)	38.4 ± 27.6	17.8 ± 32.1	0.002
Vent Days ($N = 264$)	26.5 ± 32.0	15.0 ± 23.8	0.021

were morbidly obese by definition (>100 lb over IBW). Four of 11 patients had concomitant nonburn injuries. One had penetrating abdominal trauma, whereas the other three had fractures of the spine, femur, and both pelvis and femur respectively. Nine VTE events occurred in the first 3 weeks after burn injury (See Fig. 4). There were no VTE associated deaths during this period (See Table 3).

On univariate analysis, need for ICU admission, mechanical ventilation, and ISS were found to be independently associated with VTE. Patient's age, need for prolonged air-evacuation, percent TBSA burned, presence of inhalation injury and need for surgical procedure were not associated with VTE. On multiple logistic regression analysis, the sum of ISS, and need for ICU admission was identified as being the most associated with the development VTE (See Fig. 5). Need for mechanical ventilation was also found to be a relatively strong predictor for VTE.

DISCUSSION

Air travel has long been associated with increased risk of VTE. A combination of factors such as prolonged immobilization, dehydration, and direct thrombogenic effects of hypobaric hypoxia imposed in air travel have been implicated with this increased risk.² Two recent studies highlight the ongoing debate that persists today. Schreijer et al.⁹ published recently a crossover study in 71 healthy volunteers who were subjected to an 8-hour flight, then exposed to an 8-hour movie marathon, followed by 8 hours of normal activity. Markers of coagulation and fibrinolysis were measured throughout. Authors concluded that exposure to 8 hours of flight in a Boeing 757 airplane resulted in activation of the coagulation system that was not present after the 8-hour movie marathon. This study demonstrates that conditions other than prolonged sitting such as hypobaric hypoxia may have had an effect. In a similar study, Toff et al.¹⁰ published the results of their crossover study of 73 volunteers who were all exposed alternately to 8 hours of hypobaric hypoxic conditions in a hypobaric chamber and a week later to 8 hours of normobaric normoxia. Markers of coagulation and fibrinolysis were measured serially. There were no differences noted between the two conditions. The difference in this study was that they pre-screened all participants for thrombophilias (factor V Leiden and prothrombin G20210A mutation) and excluded them whereas the former study did not. Authors concluded that in healthy patients at low risk for thrombosis, the condition of hypobaric hypoxia experienced during flight does not result in thrombo-

Table 3 Patients With VTE

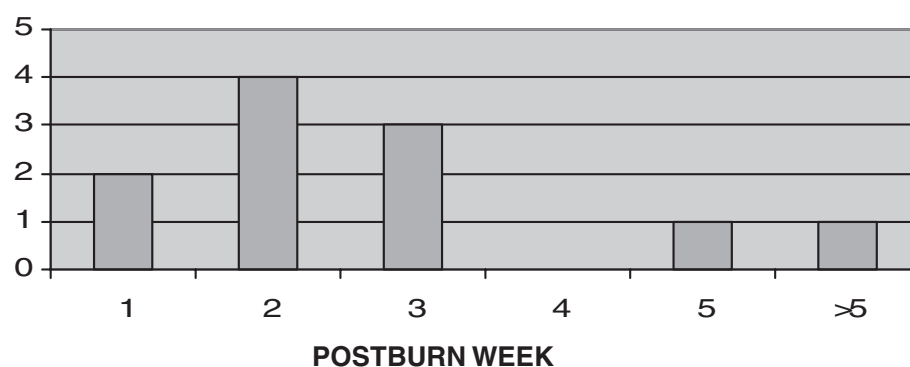
Patient†	Age	% TBSA	INH	Multitrauma	ISS	ICU Days	Vent Days	Diagnosis/Study	Survival to Discharge
1	29/M	36	Y	N	25	18	18	DVT CT angio	N
2	18/M	32	N	N	16	33	28	DVT CT angio	Y
3	46/M	39	N	N	25	45	9	PE/DVT CT angio	Y
4	45/F	55	N	N	25	28	9	PE/DVT CT angio	N
5	22/F	83	N	Y	50	112	112	DVT CT angio†	N
6	50/M	16	Y	N	13	41	36	DVT doppler US	Y
7*	36/M	8	N	Y	19	40	10	PE/DVT CT angio	Y
8*	31/M	45	Y	Y	35	26	22	PE/DVT CT angio	Y
9*	21/M	1	Y	N	10	16	13	DVT CT angio	Y
10*	25/M	33	N	Y	29	25	3	DVT CT angio†	Y
11*	26/M	5	N	N	2	0	0	PE/DVT CT angio	Y

* Military casualties.

† Incidental finding.

INH, inhalation injury.

Timing of VTE

**Fig. 4.** Nine VTE events occurred in the first 3 weeks after burn injury.

genesis. In their review, Chee and Watson² conclude that any form of travel lasting longer than 8 hours may impose an additive risk mostly in those with preexisting risk factors such as malignancy, presence of thrombophilia, or obesity. The causal role of hypobaric hypoxia and its relation to air travel and the risk of VTE appear to be weak at best but may exert the greatest effect in those at highest risk to develop clot.^{2,9-11}

Overall, there was no significant effect of global evacuation on the incidence of VTE in our study despite the military population having significantly higher ISS as well as ICU and hospital length of stay. (See Table 1). Of note, the military population also had statistically more full thickness involvement ($8.6\% \pm 17.1\%$ vs. $5.2 \pm 14.4\%$, $p = 0.001$), a higher incidence of inhalation injury (14.4% vs. 8.0% , $p < 0.0001$), and a trend toward more average major operative procedures performed (2.1 ± 2.8 vs. 1.7 ± 3.0 , $p = 0.051$) (See Table 1). Clearly the military patients were more severely injured with deeper burns, more concomitant trauma, and longer time spent lying on a hospital bed. Yet, we are surprised to see no difference in VTE incidence, especially with the added theoretical risk associated with global evacuation. There are a few possible reasons why this effect may not be apparent or may not exist at all.

First, the overall risk of VTE in burn patients is very low, making subgroup comparisons problematic. Compared with the general surgical or trauma population, burn patients have long been considered to be at relatively low risk of acquiring VTE complications. In 1988, Purdue and Hunt³ reported a 0.4% incidence of PE among 1,439 adult patients. None of the deaths were thought to be related to PE. The authors concluded that routine prophylaxis in all burn patients was not necessary unless otherwise indicated by other risk factors such as morbid obesity, lower extremity burns, or prior history of VTE. In 1992, at our institution, Rue et al.⁴ reported an overall VTE incidence of 2.1% among 2,103 patients during a span of 10 years. They also concluded that, excluding patients at highest risk, routine prophylaxis was not indicated in all burn patients. A few years later, Harrington et al.⁶ reviewed the VTE incidence again at our institution. Among 1,300 burn patients admitted in a 5 year span, the overall incidence of VTE was reported to be 2.38%. Of 31 patients with VTE, four deaths were considered to be caused by PE. They concluded that burn patients have a small increased risk of VTE and that patients advanced in age with larger burn size were at greatest risk.

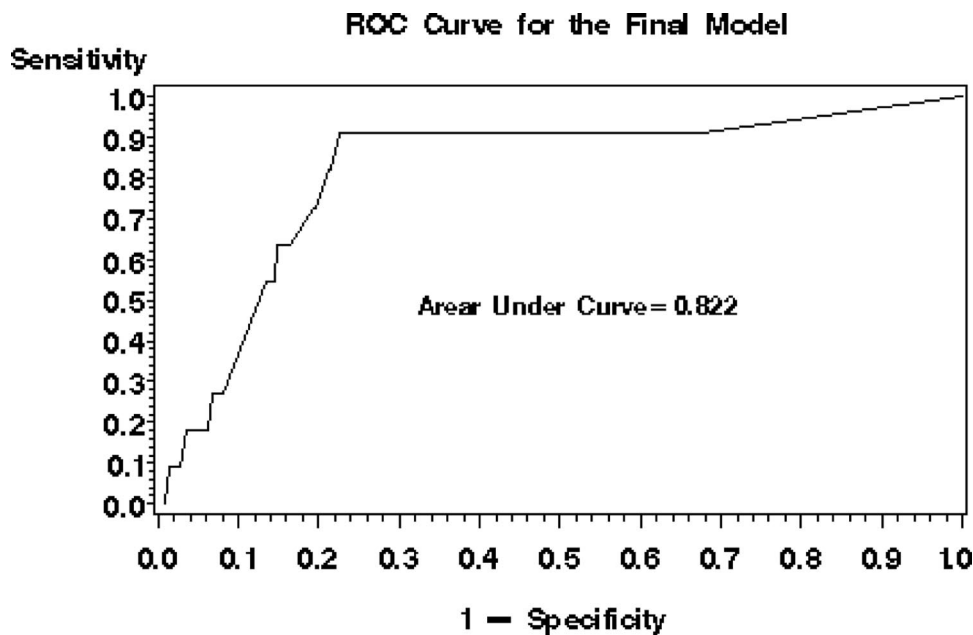


Fig. 5. ROC curve to assess the association of the SUM of ICU Admission and ISS to VTE. (95% CI for AUC: 0.67–0.97).

The low incidence of VTE is even further suppressed because of a change in practice. Because of the study by Harrington et al., it has been our standard to place all patients admitted to our burn center on chemoprophylaxis with low-molecular weight heparin unless otherwise contraindicated. In prior reviews already discussed it is not clear what percentage of their patients received some form of chemoprophylaxis. It is assumed that the percentage of patients who received some form of chemoprophylaxis was substantially lower. In addition to early walking and coordinated aggressive rehabilitation, our current standard of practice is to initiate chemoprophylaxis on all patients at the time of admission. Our standard regimen is enoxaparin 30 mg injected subcutaneously twice a day. Patients with severe renal impairment receive unfractionated heparin at 5,000 units injected subcutaneously three times a day. It is not surprising that the incidence of VTE in our institution has significantly decreased when comparing our 2 year data with the two previous reports from our institution. (0.99% vs. 2.38% and 2.1%, $p = 0.025$ and $p = 0.031$ respectively) In the military burn population, it is unclear what percentage of patients received chemoprophylaxis during their evacuation process. It is standard practice for all military medical providers to initiate chemoprophylaxis in all patients who have an indication, in accordance with the most recent national and local clinical practice guidelines.⁷ However, review of all the flight records revealed that a significant number of patients had incomplete documentation.

Although we recently reported that there are no outcome differences between civilian and combat burns, demographic differences exist.⁷ Military casualties are much younger. Although they had significantly higher ISS, incidence of inhalation injury, and ICU and hospital length of stay, these effects may not be as significant as age with regards to the

risk of VTE. The evacuated soldiers also have a low prevalence of obesity as a diagnosis. In a subgroup analysis, Harrington et al. demonstrated an increased VTE risk among obese patients, defined as $>30\%$ over IBW. A prior report by Sheridan et al. had identified morbid obesity as a significant risk factor for the development of VTE-related death in burn patients. In our study, only one patient who developed VTE was categorized as being obese during the 2-year period evaluated. None of the 11 VTE patients could be categorized as being morbidly obese. This is not surprising, as the number of morbidly obese patients admitted to our burn center is exceedingly small. In Sheridan's report, only seven patients were identified as morbidly obese during a 20-year period.¹² For these reasons comparing this population to the general civilian population is somewhat problematic.

CONCLUSION

Subjecting military burn patients, a large percentage of whom had concomitant multiple traumatic injuries, to prolonged evacuation on ground and air with combined travel times approaching 24 hours, does not result in an increase in VTE complications. A low overall incidence of VTE in burn patients, standard chemoprophylaxis, and an inherent difference in the populations compared may explain the lack of detectable difference. Our data support the continuation of our current practice of administering chemoprophylaxis in all burn patients as soon as it is clinically feasible.

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